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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/226,766	01/06/99	WANGH	L 08609/003004

HM22/0216

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EXAMINER	
CROUCH, D	
ART UNIT	**PAPER NUMBER**
1632	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/226,766	Applicant(s) Wangh
	Examiner Deborah Crouch	Group Art Unit 1632

☒ Responsive to communication(s) filed on *Nov 27, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *87-156* is/are pending in the application.

Of the above, claim(s) *142-156* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *87-141* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Applicant's arguments filed November 27, 2000 in paper no. 8 have been fully considered but they are not persuasive. The declaration by Lawrence J. Wangh, Ph.D. filed November 27, 2000 has been considered but is not persuasive as stated in the office action below. Pending claims are 87-156. Claims 87-141 are examined in this office action. Claims 142-156 have been withdrawn from consideration.

Applicant's offer of the book Genomic Potential of Differentiated Cells, by Marie A. Di Berardino, 1997, Columbia University Press, is appreciated. However, the examiner is already in possession of the book. As for the videotape, "Dawn of the Cloning Age", the Patent Office has no means to accept a videotape as evidence of enablement.

Applicant's election of group I in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 87-141 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

Claims 87-141 are drawn to the transplantation of a donor cell nucleus other than a sperm or egg nucleus into a recipient egg for the purpose of cloning, comprising an improvement where the donor-cell nucleus in incubated in cytoplasms consisting of two types 1) in a cytostatic factor-containing cytoplasm that is arrested in meiotic metaphase II or mitotic metaphase, and 2) in activated egg cytoplasm. Dependent claims address various limitations to this method, or methods implied but not stated in this method.

The examiner has read the declaration by Lawrence J. Wangh, Ph.D. as well as the attached exhibits. Dr. Wangh's historical perspective is appreciated, and the examiner has reviewed each of the references cited in parag.4-7. Agreement is reached that prior to the recent cloning events, animal cloning, and especially in mammal's, was limited to embryonic cells as nuclei donors. However, for the reasoning presented below, applicant's argument that the declaration by Dr. Wangh provides evidence for the claimed invention is not persuasive. Applicant's arguments are also not persuasive for the reasons that the declaration is not persuasive, as well as other reasons. All of applicant's arguments and statements by declarant are addressed below.

The first issue taken with Dr. Wangh's declaration, is that in U.S. Patent 5,480,772, relied upon by declarant to justify the enablement of the instant claims, all of the treatments concerned the incubation of isolate somatic cell nuclei, such as fetal erythrocytes, in two types of egg extract, an egg CSF extract and egg activating extract. There is no evidence that this type of treatment is sufficient for the nuclei to be re-programmed so that they are returned to a totipotent state. The totipotent state is required for the development of a viable animal from a somatic, differentiated or adult cell nucleus. A very important difference between applicant's invention as disclosed and that of the relevant art, is that the successful cloning using differentiated, adult or somatic cells did not incubate isolated nuclei with an extract, but inserted them into MII arrested oocytes. In fact most of the introduction of nuclei was by fusing the oocyte with a donor cell, although there was at least one report of microinjecting a nucleus into a recipient oocyte. The cloning of pigs has been particularly difficult. The particular methodologies for obtaining pigs cloned from differentiated, adult, or somatic cells is not contemplated by the instant specification. Thus, the post-filing evidence provided by applicant does not support the enablement of the instant claims. The instant specification clear contemplates animal cloning from somatic cell nuclei by the incubation of the nucleus in CSF egg extract and activating egg extract. At page 59, lines 5-19, the specification clear states "prior activation of somatic cell nuclei in an appropriate egg extract before transplanting should allow for the necessary reprogramming". At page 59, lines 14-19, state that activation of the somatic cell nucleus should be performed using the improved methods disclosed .... contacting the nucleus with activating egg

extract. The extracts are taught in the specification to be made by gathering many eggs, Xenopus to be exact, and treat them in a particular manner, break the eggs open in buffer, and after several centrifugation steps, arrive at extracts. The extracts contain supplements, and have to some extent been diluted or at least treated with buffers such that they bear little resemblance to an intact egg. There certainly is no suggestion in the specification that eggs can activate nuclear material. In addition, the methodology only applies to Xenopus, as there is no yolk in mammalian eggs. The methodology disclosed is not directly applicable to mammalian cells, and the specification provides no guidance as to the preparation of mammalian eggs to make an extract. Thus, the method disclosed in the specification is not like the ones used in the submitted prior art. The examiner could find no reference where the nuclei were incubated in CSF egg extract and then activating egg extract. Without this nexus, the suppled art is not persuasive. It is noted that declaration makes no mention in parag.15-22 of incubating isolated nuclei in two egg extracts as disclosed. The method of the specification may have used differentiated somatic cells to activate nuclear material in these cells, but the methodology is distinct from that of the post-filing art that lead to a cloned animal. There is no contemplation or enablement of claim 87 and 111. There is no evidence that the methodology of the specification provides for sufficient reprogramming to lead to a cloned animal of any species. The requirement for reprogramming is discussed in the previous office action. The statement at pages 59-60 regarding standard techniques is not supportive of incubation in a CSF containing egg followed by incubation in an activating egg.

As stated in the previous office action, the instant invention falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genetech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005).

Thus, for the reasons given above, the skilled artisan would need to engage in an undue amount of experimentation without a predictable degree of success to implement the invention as claimed as there is insufficient guidance in the specification, in view of the state of the art at the time of filing, that the claimed methods would result in nuclear reprogramming sufficient to produce by nuclear transfer a viable, term animal.

The rejection made under 35 U.S.C. 112, second parag. is withdrawn.

The claims are free of the prior art. At the time of filing, the prior art did not teach or suggest methods of nuclear transfer, where the donor nucleus was incubated first in a cytostatic egg extract and second in an activating egg extract.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

The fax number is (703) 308-4242.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

Dr. D. Crouch
February 11, 2001